

REMARKS

Claims 21-31 and 34-54 are pending, claims 25, 27, 34-36, 39 and 53 are under examination, and claims 21-24, 37, 38, 40-49, 51, 52 and 54 are withdrawn. Claims 25, 27, 34-36, 39 and 53 have been amended and claims 32 and 33 canceled by the present amendment. The amendments are supported by the specification at, *e.g.*, page 2, line 1; page 7, lines 10-13; and page 9, line 2. No new matter has been added.

Sequence Compliance

The Examiner asserts that “[a] statement did not accompany the submission of the substitute Paper Copy and Computer Readable Form of the Sequence listing, filed 7/23/02, that the substitute sequence listing did not contain New Matter” (Office Action at pages 2-3). However, both the sequence submissions of July 23, 2002, and of January 21, 2003, contained statements that the sequence listing did not contain New Matter. Applicant provides herewith copies of the two statements as filed. For emphasis, the relevant statements are boxed in the copies provided here.

Claim Objections

The Examiner objects to claim 39 as being of improper dependent form. Applicant has amended claim 39 to properly depend from claim 38, a non-elected claim, rather than from claim 27. This was an inadvertent error, the correction of which renders this objection moot.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 25-28, 32-36, 39, 50 and 53 under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner asserts that the phrase “cells that produce myoblasts” is unclear, because “[w]hile cells can be used to produce proteins, it is unclear how cells can be used to produce other cells” (Office Action at page 3). Applicant respectfully disagrees.

One of ordinary skill in the art would readily understand the fundamental events of cellular proliferation and differentiation, and would find the claims' reference to production to be clear. Moreover, the specification teaches that the claimed muscle stem cells can give rise to cells that differentiate into myoblasts (*see, e.g.*, page 7, lines 10-13). However, in the interest of advancing prosecution, Applicant has amended claims 25 and 34-36 to recite, in part, "a muscle stem cell that produces, as progeny, myoblasts". This amendment makes explicit the manner in which myoblasts are produced from the claimed cells. Thus, Applicant respectfully requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 27 and 32 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. According to the Examiner (Office Action at page 4),

Applicants claim a genus of promoters that are muscle stem cell-active....In the instant case, applicants teach that a promoter active in a muscle stem cell can direct transcription in a muscle stem cell. Expression of a reporter gene is considered an indication that the promoter is active in muscle stem cells (*see e.g.* bridging paragraph page 5-6). Bcl-2 promoters are specifically disclosed as appropriate for this purpose. Neither applicant nor the prior art provide a correlation between the bcl-2 promoter and their muscle stem cell activity. Given the large size and diverse nature of promoters, and the inability to determine which will also possess muscle stem cell activity, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of the claimed genus.

Applicant respectfully disagrees. First, Applicant has described more than one species of muscle stem cell-active promoter. For example, the specification teaches that nestin and desmin promoters can be used, either alone or in conjunction with the bcl-2 promoter, to express an exogenous coding sequence (*see, e.g.*, page 20, lines 9-11). Second, the *Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, paragraph 1 "Written Description" Requirement* (Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001)

provide that "what constitutes a 'representative number' is an inverse function of the skill and knowledge of the art." In the present case, the skill and knowledge of one of ordinary skill in the art is high; certainly high enough to select a promoter to express a protein in a given cell type. It was routine in the art at the time the present application was filed to use cell type-specific promoters, and methods were known at that time that could be used to identify other promoters active in muscle stem cells (*e.g.*, subtractive cDNA hybridization and differential display).

Finally, contrary to the Examiner's assertion, the specification describes a direct correlation between the bcl-2 promoter and muscle stem cell activity. The Examples demonstrate that the bcl-2 promoter directs exogenous protein expression in muscle stem cells (*see, e.g.*, page 30, lines 13-17; page 30, line 23 to page 31, line 9; and page 31, lines 11-19). Thus, Applicant has established that the bcl-2 promoter is active in muscle stem cells. In view of the knowledge and level of skill in the art at the time of filing, the disclosure of three species of promoters that can direct protein expression in muscle stem cells, the availability of methods to identify muscle stem cell-specific promoters, and the demonstrated activity of a bcl-2 promoter in the claimed cell type, one of ordinary skill in the art would recognize that Applicant was in possession of the full scope of the invention now claimed. Accordingly, claim 27 complies with the written description requirement.

Although Applicant disagrees that claim 32 fails to comply with the written description requirement, Applicant has canceled claim 32 (and dependent claim 33), rendering this rejection moot.

Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 25-27, 32-36, 50 and 54¹ under 35 U.S.C. § 102(b) as anticipated by Wang *et al.* (*Growth Factors* 9:57-71, 1993, hereinafter "Wang"), in view of Gazit *et al.* (*Mol. Endo.* 7:189-98, 1993, hereinafter "Gazit"). According to the Examiner (Office Action at page 6),

¹ Although the Examiner rejected claim 54, Applicant believes the Office Action contained an error, and that the rejection should be applied instead to claim 53. Claim 54 is withdrawn as a non-elected claim, and the Examiner's remarks are appropriate for claim 53. Confirmation is respectfully requested..

Applicant : Jeffrey B. Miller
Serial No. : 09/909,237
Filed : July 19, 2001
Page : 9 of 9

Attorney's Docket No.: 08472-720003 / MGH-1176.2
Miller - Cont.

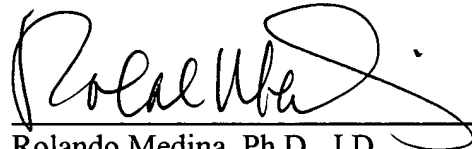
Wang et al teach transfection of C3H-10T1/2 cells, a clonal cell line prepared from mouse embryo cells, with BMP-2 cDNA. BMP2 expression is indicative of the promoters operably linked to the coding sequence activity in muscle stem cells. Gazit et al teach that mesenchymal stem cells give rise to myoblasts (see e.g. abstract). Hence mesenchymal stem cell lines such as C3H-10T1/2 are muscle stem cells that lead to myoblast cells (emphasis added).

This rejection should be withdrawn in view of the present amendment of claims 25, 34-36, and 53 to recite "human muscle stem cells". In order to anticipate the claims, all the limitations of the present claims must be disclosed by the cited references. As neither Wang nor Gazit teach human muscle stem cells, neither Wang nor Gazit can anticipate the present claims. Thus, Applicant respectfully requests that the Examiner withdraw this rejection.

Enclosed is a Petition for Extension of Time fee along with the required fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 1 September 2004



Rolando Medina, Ph.D., J.D.
Reg. No. 54,756

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906